

What is claimed is:

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1. A method of reducing or inhibiting angiogenesis in a tissue, comprising contacting  $\alpha 5 \beta 1$  integrin in the tissue with an agent that interferes with  
5 specific binding of the  $\alpha 5 \beta 1$  integrin to a ligand expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue.

2. The method of claim 1, wherein the agent does not substantially interfere with the specific binding  
10 of a ligand to an integrin other than  $\alpha 5 \beta 1$  integrin to its ligand.

3. The method of claim 1, wherein the ligand is fibronectin.

4. The method of claim 1, wherein the tissue  
15 comprises ocular tissue.

5. The method of claim 4, wherein the ocular tissue is selected from the group consisting of retina, macula and cornea.

6. The method of claim 1, wherein the tissue  
20 comprises skin.

7. The method of claim 1, wherein the tissue comprises synovial tissue.

8. The method of claim 1, wherein the tissue comprises bone.

25 9. The method of claim 1, wherein the tissue comprises a neoplasm.

10. The method of claim 9, wherein the neoplasm is a malignant neoplasm.

11. The method of claim 10, wherein the malignant neoplasm is a metastatic malignant neoplasm.

5 12. The method of claim 10, wherein the malignant neoplasm is a carcinoma.

*mb c2* 13. The method of claim 1, wherein the agent comprises a peptide.

10 14. The method of claim 13, wherein the peptide comprises the amino acid sequence CRRETAWAC (SEQ ID NO: 1).

15 15. The method of claim 1, wherein the agent comprises an anti- $\alpha 5 \beta 1$  integrin antibody or an  $\alpha 5 \beta 1$  integrin binding fragment of said antibody.

16 16. The method of claim 1, wherein the agent comprises a nonpeptide organic molecule.

17. The method of claim 16, wherein the nonpeptide organic molecule is a heterocycle having the general structure (S)-2-phenylsulfonylamino-3-  
20 {{{8-(2-pyridinyl aminomethyl)-}-1-oxa-2-azaspiro-{4,5}-dec-2-en-yl} carbonylamino}propionic acid.

18. The method of claim 16, wherein the nonpeptide organic molecule comprises  
(S)-2-{{(2,4,6-trimethylphenyl)sulfonyl}amino-3-  
25 {7-benzyloxycarbonyl-8-(2-pyridinylaminomethyl)-1-oxy-2,7-diazaspiro-{4,4}-non-2-en-3-yl}carbonylamino}  
propionic acid.

19. The method of claim 1, wherein the agent is linked to a cytotoxin.

20. The method of claim 19, wherein the cytotoxin is a cancer chemotherapeutic drug.

21. A method of identifying the presence of angiogenesis in a tissue, comprising the steps of:

a) contacting the tissue with an agent that specifically binds  $\alpha 5 \beta 1$  integrin, and

b) detecting specific binding of the agent to  $\alpha 5 \beta 1$  integrin associated with a blood vessel in the tissue, thereby identifying the presence of angiogenesis in the tissue.

22. The method of claim 21, wherein the agent comprises a peptide.

23. The method of claim 21, wherein the agent comprises the amino acid sequence CRRETAWAC (SEQ ID NO: 1).

24. The method of claim 21, wherein the agent comprises an anti- $\alpha 5 \beta 1$  integrin antibody or an  $\alpha 5 \beta 1$  integrin binding fragment of said antibody.

25. The method of claim 21, wherein the agent comprises a nonpeptide organic molecule.

26. The method of claim 25, wherein the nonpeptide organic molecule is a heterocycle having the general structure (S)-2-phenylsulfonylamino-3-  
{{{8-(2-pyridinyl aminomethyl)}-1-oxa-2-azaspiro-  
{4,5}-dec-2-en-yl} carbonylamino}propionic acid.

27. The method of claim 25, wherein the non-peptide organic molecule comprises (S)-2-((2,4,6-trimethylphenyl)sulfonyl)amino-3-  
{7-benzyloxycarbonyl-8-(2-pyridinylaminomethyl)-  
5 1-oxy-2,7-diazaspiro-{4,4}-non-2-en-3-yl}carbonylamino}  
propionic acid.

28. The method of claim 21, wherein the agent further comprises a detectable label.

29. The method of claim 21, wherein detecting  
10 specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue comprises the steps of:

15 a) contacting the agent, which is specifically bound to  $\alpha 5\beta 1$  integrin, with a reagent that specifically interacts the agent, and

b) detecting interaction of the reagent, thereby detecting specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue.

20 30. The method of claim 21, wherein the tissue is selected from the group consisting of embryonic tissue and placental tissue.

31. The method of claim 21, wherein the tissue comprises granulation tissue.

25 32. The method of claim 21, wherein the tissue is involved in a pathological condition.

33. The method of claim 32, wherein the pathological condition comprises a neoplasm.

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34. The method of claim 32, wherein the tissue comprises ocular tissue.

35. A method of diagnosing a pathological condition characterized by angiogenesis in a tissue in an individual, comprising the steps of:

a) obtaining a sample of the tissue from the individual, wherein, in an individual having the pathological condition, the tissue exhibits angiogenesis;

10 b) contacting the sample with an agent that specifically binds  $\alpha 5\beta 1$  integrin; and

15 c) detecting specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue, thereby diagnosing a pathological condition characterized by angiogenesis in the individual.

36. The method of claim 35, wherein the pathological condition involves the eye.

20 37. The method of claim 36, wherein the pathological condition is selected from the group consisting of diabetic retinopathy and macular degeneration by neovascularization.

38. The method of claim 35, wherein the pathological condition involves the skin.

25 39. The method of claim 38, wherein the pathological condition is selected from the group consisting of a hemangioma and psoriasis.

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40. The method of claim 35, wherein the pathological condition involves a joint.

41. The method of claim 40, wherein the pathological condition is selected from the group consisting of rheumatoid arthritis and osteoarthritis.

42. The method of claim 33, wherein the pathological condition involves a neoplasm.

43. The method of claim 42, wherein the neoplasm is a malignant neoplasm.

44. The method of claim 43, wherein the malignant neoplasm is a metastatic malignant neoplasm.

45. The method of claim 43, wherein the malignant neoplasm is a carcinoma.

46. The method of claim 45, wherein the carcinoma is selected from the group consisting of breast carcinoma, colon carcinoma, ovarian carcinoma, and pancreatic carcinoma.

47. A method of diagnosing a pathological condition characterized by angiogenesis in a tissue in an individual, comprising the steps of:

a) administering an agent that specifically binds  $\alpha 5 \beta 1$  integrin to an individual suspected of having the pathological condition; and

5           b) detecting specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue, thereby diagnosing a pathological condition characterized by angiogenesis in the individual.

48. The method of claim 47 wherein the agent is detectably labeled.

49. The method of claim 48, wherein detecting specific binding of the agent is performed using an  
10 *in vivo* imaging method.

50. The method of claim 48, wherein the detectably labeled agent comprises the agent linked to a label selected from the group consisting of a radionuclide, a paramagnetic material and an X-ray  
15 attenuating material.

51. The method of claim 49, wherein the *in vivo* imaging method is selected from the group consisting of radionuclide imaging, positron emission tomography, computerized axial tomography, and magnetic  
20 resonance imaging.

52. The method of claim 48, wherein detecting specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue comprises the steps of:

25           a) obtaining a sample of the tissue from the individual; and

          b) detecting specific binding of the agent in the sample.

53. The method of claim 47, wherein detecting specific binding of the agent to  $\alpha 5\beta 1$  integrin associated with a blood vessel in the tissue comprises the steps of:

5 a) obtaining a sample of the tissue from the individual;

b) contacting the agent that is specifically bound to  $\alpha 5\beta 1$  integrin with a reagent that specifically interacts with the agent; and

10 c) detecting interaction of the reagent with the agent, thereby diagnosing a pathological condition characterized by angiogenesis in the individual.

15 54. The method of claim 47, wherein the individual is a human.

55. A method of reducing or inhibiting angiogenesis in a tissue in an individual, comprising administering to the individual an agent that interferes with the specific binding of  $\alpha 5\beta 1$  integrin to a ligand  
20 expressed in the tissue, thereby reducing or inhibiting angiogenesis in the tissue in the individual.

56. The method of claim 55, wherein the individual is a human.



57. A method of reducing the severity of a pathological condition associated with angiogenesis in an individual, comprising administering to the individual an agent that interferes with specific binding of  $\alpha 5 \beta 1$  integrin to a ligand in a tissue associated with the pathological condition, thereby reducing or inhibiting angiogenesis in the tissue, and reducing the severity of the pathological condition.

58. The method of claim 57, wherein the pathological condition is a neoplasm.

59. The method of claim 58, wherein the neoplasm is a malignant neoplasm.

60. The method of claim 59, wherein the malignant neoplasm is a metastatic malignant neoplasm.

61. The method of claim 59, wherein the malignant neoplasm is a carcinoma.

62. The method of claim 61, wherein the carcinoma is selected from the group consisting of a breast carcinoma, a colon carcinoma, an ovarian carcinoma and a pancreatic carcinoma.

63. The method of claim 59, wherein the malignant neoplasm is selected from the group consisting of a sarcoma, a mesothelioma, a teratocarcinoma, an astrocytoma, and a glioblastoma.

64. The method of claim 57, wherein the individual is a human.

65. The method of claim 57, wherein the agent is administered intravenously.

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66. The method of claim 57, wherein the agent is administered orally.

67. The method of claim 58, wherein the agent is administered into a neoplasm.

5 68. The method of claim 57, wherein the pathological condition is associated with the eye.

69. The method of claim 68, wherein the pathological condition is selected from the group consisting of diabetic retinopathy and macular  
10 degeneration by neovascularization.

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70. The method of claim 68, wherein the agent is administered in the form of eye drops.

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71. The method of claim 68, wherein the agent is administered intravenously.

15 72. The method of claim 68, wherein the agent is administered orally.

73. The method of claim 57, wherein the pathological condition is associated with a joint.

74. The method of claim 73, wherein the agent  
20 is administered intrasynovially.

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75. The method of claim 57, wherein the agent is administered at a dose of 0.0001 to 100 mg/kg body weight.

76. A method of identifying an agent that reduces or inhibits angiogenesis associated with  $\alpha 5 \beta 1$  integrin expression in a tissue, comprising the steps of:

5 a) contacting a tissue exhibiting angiogenesis associated with  $\alpha 5 \beta 1$  integrin expression with an agent; and

10 b) detecting a reduction or inhibition of angiogenesis in the tissue, thereby identifying an agent that reduces or inhibits angiogenesis associated with  $\alpha 5 \beta 1$  integrin expression in a tissue.

77. The method of claim 76, wherein contacting the tissue occurs *in vivo*.

15 78. The method of claim 76, wherein contacting the tissue occurs *ex vivo*.

79. The method of claim 76, wherein the tissue comprises malignant neoplastic tissue.

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